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13. ABSTRACT (Maximum 200 Words)

The goals of the study are to evaluate the role of paravertebral blocks regional anesthesia in patients undergoing operative treatment of breast cancer. Experience to date has shown that this anesthetic modality is safe and effective, and associated with excellent post operative pain control and minimization of nausea and vomiting associated with general anesthesia. Using a prospective randomized trial carried out at two institutions, we propose to measure quality of life variables including pain, postoperative nausea an vomiting, mood, and functional status in patients undergoing breast surgery with the traditional techniques of general anesthesia versus the region technique of paravertebral block.

The preliminary phase of this trial, which establishes the safety and efficacy of performing the block technique, is complete. We are currently in the study portion of the trial and have consented and randomized a total of 35 patients at one institution thus far. Outcomes and study instruments are detailed in the report. Our collaborating institution, the Mayo Clinic Jacksonville, is awaiting final institutional approval in order to begin recruiting patients.

14. SUBJECT TERMS
breast cancer, paravertebral block anesthesia, breast cancer surgery postoperative pain, nausea and vomiting, quality of life

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INTRODUCTION

General anesthesia is currently the standard anesthetic technique used for modified radical mastectomy, lumpectomy with axillary dissection, and other major operations performed for the treatment of breast cancer. While general anesthesia ensures tolerance of the operative procedure, it is associated with a high incidence of postoperative nausea and vomiting in patients undergoing breast surgery and it is not capable of providing pain relief following emergency. Treatment of pain with parenteral narcotics and supportive care of postoperative nausea prolong hospitalization and diminish quality of life following breast cancer surgery. Paravertebral block is a regional anesthetic technique used historically for the diagnosis and treatment of chronic somatic pain and for operative procedures for the chest and shoulder. The concept of using paravertebral block anesthesia for breast surgery was introduced at Duke University Medical Center in 1994 with the goals of providing safe and effective anesthesia, prolonged postoperative pain relief, reduced nausea and vomiting, and thus improved quality of life following surgical treatment of breast cancer. Retrospective review of a three-year experience with this technique has shown that these goals are being realized (see attached *Annals of Surgery* article). The block provides effective anesthesia in 85% of cases and has a low complication rate of 2.6%. The technique provides sensory block that persists for an average of 23 hours, and therefore the patient experiences minimal surgical pain. Compared to general anesthesia, inpatient narcotic use in those undergoing paravertbral block is reduced from 98% to 25% while anti-emetic use in those undergoing paravertebral block is reduced from 39% to 20%. Patient satisfaction is high, hospital stays are shortened, and we now consider paravertebral block the anesthetic of choice for operative treatment of breast cancer. To test this hypothesis we proposed a prospective randomized clinical trial comparing general anesthesia and paravertebral block. The protocol for this trial was designed such that all aspects perioperative patient care other than the anesthetic used during surgery will be uniform. Narcotic, anti-emetic, and other medication use and responses to questionnaires measure pain, nausea, mood, and other quality of life outcomes during the postoperative interval. Our goal is to definitively evaluate paravertebral block anesthesia in this application and to facilitate widespread use of a new technique that will markedly improve quality of life for most patients with breast cancer.

GCO # 97-368

PROGRESS REPORT

- **Task 1. Establish anesthesiologists' proficiency in performing paravertebral block.**
- **Status. Complete**

In April of 1999 Dr. Victor Moreno of the Department of Anesthesiology, Mount Sinai Medical Center, traveled to Duke University Medical Center to study the paravertebral block technique. Under the supervision of Dr. Roy Greengrass, Dr. Moreno attained preliminary proficiency sufficient to perform this block independently and train other anesthesiologist. During the subsequent months Dr. Moreno and colleagues performed ten paravertebral blocks on patients undergoing either modified radical mastectomy or lumpectomy with axillary lymph node dissection for the surgical treatment of breast cancer. The efficacy rate of these blocks was 70%; in three cases conversion to general anesthesia was required due to inadequate block at all levels. No complications were encountered while performing these blocks including pneumothorax, infection, intravascular injection of local anesthetic, or epidural spread. Unfortunately in January of 2000 Dr. Moreno left the faculty of Mt. Sinai Medical Center thereby delaying scheduled progress according to the original statement of work. Dr. Janet Pittman from the Department of Anesthesiology at Mt. Sinai Medical Center has taken Dr. Moreno's place in this role. Dr. Pittman was likewise trained in the paravertebral technique under the supervision of Dr. Greengrass at Duke University. She currently employs this technique at Mt. Sinai, has established its safety and efficacy and has trained one additional colleague, Dr. Barabara Dillos, also of the Mount Sinai Department of Anesthesiology.

Due to the change in personnel, we anticipated a delay of approximately 10 months in completion of tasks II and III as outlined in the Statement of Work, and so requested (and were granted), a no-cost 18-month extension to the schedule of this trial. The operational period was extended to October 2002, with an effective study start date of February 2000. Accordingly, this report reviews the complete accomplishments to date, and moreover, highlights the progress of the research activities since the progress report filed with the IRB last year.

- **Task 2. Preparation of study materials and training of study coordinators.**
- **Status. Complete**

The study's existing part-time Clinical Trial Coordinator, Mr. John Arbo, was enlisted full-time in June of 2001. Mr. Arbo has been affiliated with the Department of Surgery at Mount Sinai since January of 2000, when he was brought on part-time to finalize the study's questionnaires, patient consent forms, and study

protocol. Mr. Arbo worked closely with Dr. Guy Montgomery of Mount Sinai's Ruttenberg Cancer Center in order to develop an appropriate and comprehensive patient questionnaire. Mr. Arbo also worked closely with Dr. Maryann Pranulis, the U.S. Army's Human Subjects Protection Specialist assigned to this study, in order to finalize the study's protocol and patient consent forms. Protocol amendments received final approval from the U.S. Army Human Subjects Protection Board on June 19, 2001. In preparation for his responsibilities as Trial Coordinator, Mr. Arbo also completed Mount Sinai's certification course in Protection in Human Subjects in Research on June 6, 2001. Mr. Arbo received additional training and authorization to prepare patients for completing study questionnaires and for administering study consent forms. Mr. Arbo holds a Masters degree from Columbia University, has significant health care and database management experience, and is well versed in the intricacies of this particular study. He will remain with the study until its completion, and will contribute to the final analysis and presentation efforts.

- **Task 3. Subject recruitment and randomization, execution of study protocol, completion of questionnaires.**
- **Status: Ongoing**

The departure of additional participating personnel within the surgical faculty at Mt. Sinai has reduced the anticipated number of patients that will be recruited into the trial at this center. Similarly delays in patient recruitment occurred on account of Dr. Greengrass's departure from Duke University for his new position with the Department of Anesthesiology at the Mayo Clinic Jacksonville. Dr. Greengrass has received final IRB/Army approval for his site-specific protocols and consent form at the Mayo Clinic.

Patient recruitment at Mount Sinai began in June of 2001. Although initially slow, our recruitment rate has increased, with a total of 29 patients recruited as of November 2002. Study protocol has been successfully executed in all areas, as has completion of study questionnaires and statistical analysis of perioperative data. This enrollment rate, together with expected enrollment at the Mayo Clinic, should provide the necessary number of patients to complete the study. Current results, including negative as well as positive findings are reported below.

- **Task 4. Data analysis, preparation of reports.**
- **Status. Ongoing**

Since June 2001, a total of 35 patients have been consented for participation in the study. Of these 35, 33 were scheduled for lumpectomy with axillary node dissection (LAD), and 2 for modified radical mastectomy

(MRM). Of the 33 patients scheduled for LAD, 2 were disqualified from the study during the previous year, as already reported: the first patient (randomized to receive the block) was disqualified after being identified as having a schizophrenic disorder that prevented her from completing the questionnaires in an objective manner. The patient's disorder was identified after completion of surgery. The surgery was completed without event, and the patient's questionnaire responses were not entered into the database. The second patient (also randomized to the block) was disqualified on account of an adverse event unrelated to the block. Conversion to Monitored Anesthetic Care was required. The patient's surgery was completed without event, and no post-surgery questionnaires were completed. Details of this adverse event were reported to appropriate personnel at the Mount Sinai IRB and U.S. Army in a timely and comprehensive manner. A copy of the Adverse Event report is on file with the Mt. Sinai IRB. No patients were disqualified during the period of November 2001 – September 2003, and there are no new adverse events to report to date.

However, it should be explicitly noted that during this year, we made the decision to discontinue the procedure of modified radical mastectomies for this study. Reconstruction was a disqualification factor, and because there are so few patients who undergo a mastectomy without a reconstruction, we realized that we could not recruit enough patients to achieve statistically meaningful numbers if we included those undergoing mastectomies without reconstruction. Furthermore, because modified radical mastectomy versus lumpectomy with axillary node dissection stratification was another criterion for the study, we could not lump the two procedures together and analyze the data accordingly. Thus, we made the decision to pursue LADs only for this study.

Accordingly, the following numbers represent the number of qualified patients since June 2001:

Patients undergoing lumpectomy with axillary node dissection:	*2/2000 – 12/2002*	*1/2003 – 9/2003*
Total number of patients randomized to GA	13	4
Total number of patients randomized to PVB	12	2
Patients undergoing modified radical mastectomy:		
Total number of patients randomized to GA	1	0
Total number of patients randomized to PVB	1	0
Total number of patients:	27	6

With these figures documented, the following reportable data from the initial 25 qualified LAD patients completing questionnaires can be summarized as follows:

Average pain score (Memorial Symptom Assessment Scale 1-4) for patients undergoing LAD:

	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Paravertebral Block	2.6	2.1	1.8	1.1	1.4	1.2	1.5	1.6
General Anesthesia	2.9	1.6	1.6	2.0	1.3	1.2	0.9	1.0

Average pain score (Visual Analogue Scale 0-10) for patients undergoing LAD:

	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Paravertebral Block	3.4	3.5	1.9	1.7	1.4	1.4	1.6	1.9
General Anesthesia	4.2	2.3	3.0	4.0	3.0	2.3	2.3	2.0

Average nausea score (Memorial Symptom Assessment Scale 1-4) for patients undergoing LAD:

	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Paravertebral Block	1.4	1.3	0.4	0.3	0.0	0.1	0.1	0.0
General Anesthesia	2.4	1.0	0.1	0.1	0.0	0.0	0.1	0.1

Average nausea score (Visual Analogue Scale 0-10) for patients undergoing LAD:

	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Paravertebral Block	2.0	1.6	0.6	0.2	0.0	0.0	0.0	0.0
General Anesthesia	3.4	0.7	0.4	0.1	0.1	0.0	0.0	0.0

Preliminary statistical analysis of limited perioperative data has been completed for the study's initial 25 qualified LAD patients. Comprehensive analysis of patient questionnaires and perioperative data will be reserved until completion of the trial. However, preliminary sample statistical review was conducted in May 2002 to evaluate results of the study to date. The following was documented:

Preliminary Sample Data Analysis as of May 2002

	PBV	GA	Notes
Percentage of patients discharged from PACU	83%	22%	
1:15min post-surgery VAS (0-10 pain score)	3.5	5.9	40% reduction
1:15min post-surgery MSAS (1=slight, 4=very severe)	1.43	2.6	45% reduction
1:15min post-surgery pain med usage	1.0	2.86	65% reduction
Average patient satisfaction overall care (1=excellent 5=poor)	1.57	1.5	

All study patients have reported a high level of satisfaction with all aspects of their surgery, study staff, and hospital care. The current low number of patients enrolled allows us to do only limited statistical power analysis. We anticipate that as enrollment increases, pain and nausea scores will approximate previous results from the original Duke University case study. More rigorous statistical analysis will be conducted as more data is made available.

Key Research Accomplishments

- Employment of full-time Clinical Trial Coordinator for Mount Sinai.
- Poster presentation by Mount Sinai staff of study goals and methods at a Department of Defense funded Era of Hope Breast Cancer Conference, Atlanta, June 8-11, 2000.
- IRB/Army approval of Mount Sinai revised protocol, patient questionnaires, and consent form.
- Initiation of patient recruitment at Mount Sinai.
- Continuation of recruitment at Mount Sinai (35 patients total).
- Initial statistical analysis of perioperative results from first 25 qualified LAD Mount Sinai study patients.
- Mayo Clinic Jacksonville (collaborating research institution) IRB/Army approval of site-specific protocol.

Reportable Outcomes

- Poster presentation by Mount Sinai staff of study goals and methods at a Department of Defense funded Era of Hope Breast Cancer Conference, Atlanta, June 8-11, 2000.

No other reportable outcomes at this time.

Conclusions

Excellent progress has been made in initiating patient recruitment at the Mount Sinai Medical Center. Study protocol, patient questionnaires, and consent forms are being implemented successfully, patient satisfaction is high, and patient enrollment is up. The decision to discontinue modified radical mastectomies, as previously noted, was made when we realized that we could not recruit enough patients to achieve statistically meaningful numbers if we included those undergoing mastectomies without reconstruction. This will influence neither the tangible reportable outcomes, nor importance, of the study. Anticipated obstacles to patient recruitment due to departure of personnel as noted in the previous progress report are still being dealt with satisfactorily. At this time, given the limited number of patients enrolled in to the study, only limited statistical analysis of perioperative results can be made. However, to date, all study patients have reported a high level of satisfaction with all aspects of their surgery, study staff, and hospital care. We anticipate that as enrollment increases, pain and nausea scores will approximate previous results from the original Duke University case study. More rigorous statistical analysis will be conducted as more data is made available, and the importance and implications of trial results will be determined following additional patient recruitment.

REFERENCES

1. Weltz CR, Greengrass RA, Lyerly HK. Ambulatory Surgical Management of Breast Carcinoma Using Paravertebral Block. Ann Surg 1995; 222:19026

APPENDIX

Attachments:

- Copy of revised and IRB approved study protocol for continuing trials
- Copy of revised and IRB approved consent form for continuing trials

PROTOCOL SUMMARY FOR NEW AND CONTINUING PROTOCOLS

1. Provide a brief (200-250 word) summary of background information for physicians/scientists:

Paravertebral block anesthesia is a regional techniques in which local anesthesia is injected into paravertebral space, the area immediately lateral to the spinal cord where spinal nerves emerge from the intervertebral foraminia. Attributes of this anesthesia included ease of administration, low morbidity, and potential for prolonged sensory block and prolonged relief due to the relative avascularity of the paravertebral space. This technique is used widely inoperative procedures of the chest or trunk; however, it has only been used in breast surgery since 1994 by collaborating anesthesiologists and surgeons at Duke university medical center. Their experience confirms the technique's safety and efficacy in over 250 cases to date. Significant differences in postoperative pain, nausea and vomiting, and length of hospital stay were detected when paravertebral block was compared to general anesthesia.

2. State purpose of study:

The purpose of this study is to measure quality of life variable of pain, nausea, and vomiting, mood, and functional status in patients during the interval following breast surgery with the traditional techniques of general anesthesia versus the new regional technique paravertebral block. It is hypothesized that significant differences in postoperative pain, nausea, and vomiting, and length of hospital stay will be detected. We also hypothesize that quality of life as measured by functional status, mood a, and return to work and normal activities will be improved in patients undergoing paravertebral block anesthesia. Specifically, we will, 1) determine the safety and efficacy of paravertebral block as an anesthesia techniques for procedures of the breast an axilla, 2) compare the incidence, severity and duration of postoperative pain and other side effects and, 3) assess the ability to perform breast surgery on an ambulatory or 0vernight basis and; compare mood and functional status between paravertebral block anesthesia and general anesthesia.

3. Indicate number of subjects to be enrolled at this site: 40
Indicate total number of subjects to be enrolled, if multicenter study: 75

4. Indicate the characteristics of study population:

(a) Gender:	Males	yes_____	no_____
	Females	yes__x__	no_____
(b) Age range:		from 18	to 75
(c) Racial and Ethnic Groups:			
	Caucasian	yes___x__	no_____
	Black	yes___x__	no_____
	Hispanic	yes___x__	no_____
	American Indian	yes___x__	no_____
	Alaskan Native	yes___x__	no_____
	Asian/Pacific Islander	yes___x__	no_____
	Other (specify):		

(d) Justify any exclusion of specific gender, age, and racial or ethnic groups: N/A

5. State inclusion criteria for enrollment in study:

- Diagnosis of invasive breast cancer
- Planned surgery (lumpectomy with axillary dissection)
- Able and willing to give informed consent.
- Agree to complete requirements of the study.

6. State exclusion criteria for enrollment in study:

- Patients with contraindications to placement of paravertebral block; i.e., coagulopathy, chronic progressive neuropath or infections at proposed injection site.
- Patients undergoing bilateral resection or mastectomy following reconstruction.
- Pregnant patients.
- Patients without an adequate command of the English language.

7. Will vulnerable subjects be enrolled in this study?	yes__x__	no_____
(a) Individuals with diminished mental capacity	yes_____	no___x__
(b) children	yes_____	no___x__
(c) pregnant women	yes_____	no___x__
(d) fetuses	yes_____	no___x__
(e) economically or socially disadvantaged persons	yes__x__	no_____
(f) prisoners	yes_____	no___x__

8. If vulnerable subjects are to be enrolled, describe the special precautions that will be taken to ensure that consent is freely given and that the rights and welfare of the subjects are protected:

Economically and socially disadvantaged subjects will not be excluded from the study. A patient's financial status will not impact her ability to participate in the study. The study will not incur additional costs, and patients will be responsible for the costs of surgery and anesthesia in the same manner as if they were not participating in the research study.

9. If the study involves children, will the MSSM Certification of Assent form be used to document that assent was freely given without coercion? yes___ no____

If no, indicate how assent will be documented: N/A

10. Indicate where and how research data will be stored to ensure confidentiality:

Collected data will be stored in locked file cabinets in the Department of Surgery Administrative Offices of the 15th floor, 5 East 98th Street. Patients will be given a code number and these numbers will be used as identifiers through out the study. The list of research code numbers will be maintained by the Principal Investigator and/or Project Coordinator. The research data will be separate from the clinical data, and the coded link which correlates the identifying information and the research code the will be stored on a password protected laptop computer. The computer is not linked to a network, and it will be stored in locked file cabinet in a locked office. The Principal Investigate and/or Project Coordinator will have access to the link.

11. Will data (e.g. records, samples, specimens, databases, surveys, etc.) be *obtained* with identifiers that can be directly or indirectly linked back to the subjects?

yes__x___ no_____

12. Will data (e.g. records, samples, specimens, databases, surveys, etc.) be *stored* with identifiers that can be directly or indirectly linked back to the subjects?

yes__x___ no_____

13. Indicate who will have access to information about the subjects that is identifiable:

The Principal Investigator and/or Project Coordinator will have access to identifiable information. In the event that other study personnel require access, the principal investigator will review the circumstances individually.

14. Indicate how potential subjects will be identified and recruited for participation in the study:

Candidates for the study will be identified by the Principal Investigator and recruited. Other surgeons will be approached concerning the study, and they will select appropriate candidates from their individual practices or clinics. Potential subjects will be given the name and phone number of the Project Coordinator to call if they are interested in participating in the study.

15. Indicate when and where consent will be obtained:

The criteria for participation are the diagnosis of invasive breast cancer and a planned surgical treatment (lumpectomy with axillary dissection). Additional screening procedures to determine if a patient qualifies as a study participant are not applicable to this study. Potential subjects will not undergo additional tests, nor be exposed to any potential risks to determine their ability to participate. If the study candidate meets the inclusion criteria, the surgeon and/or study personnel so designated will explain and obtain consent prior to surgery. The patient will be afforded a private room in the clinic to read this consent form, or have it read to her. This space will be made available to the patient for as long as she requires to review the consent form in its entirety.

16. Indicate how you will determine whether the subjects understand the information that was provided in the consent document:

During an information session with the candidate, designated study personnel will go over the consent page by page. It is not expected that the subject will be unable to sign for herself, but in the event that a physical inability prevents the patient from penning her own signature, a verbal indication of consent will be sought. To ensure that the subjects understand they will be asked to reiterate in their own words the purpose of the research, what they will need to do as participants in the study and what the potential risks, benefits and alternatives are. This study will not use surrogates, and study personnel will obtain written consent (or verbal consent in circumstances of physical inability) directly from the subject as previously articulated.

17. Will the study include medical record review (hard copy of record or via computer)?

yes__x___ no_____

If yes, list those individuals (e.g. co-investigators, fellows, research nurses, research coordinators, pharmaceutical company protocol monitors, etc.) who require access to the record:

Title	Dept./Institution/Company
Principal Investigator/Co-Ivest.	Surgery/Anesthesia
Research Coordinator	Surgery
Government Monitor	Department of the Army

18. Narrative Summary

The administration of the paravertebral block anesthesia is being done for research purposed along with assessments of well being after the surgery. Otherwise, the surgery and all the testing will be done as if the patient was not participating in a study. The tests and procedures done for the aforementioned research purposes include the administration of the paravertebral block anesthesia, a patient diary and finally a telephone survey to perform questionnaires on pain, nausea and vomiting, and mod during a six day postoperative period, seventh day following surgery, and at week four to see if the patient has returned to normal activities or work. The data will be collected and analyzed so that comparisons can be made between general anesthesia and paravertebral block and the impact on quality of life. Patients who elect to participate will incur no charge other than those they would normally incur when under surgery for invasive breast cancer. Anesthesia charges for either procedure will be comparable. Likewise, all patients will receive Vioxx for initial pain treatment in the PACU, and discharge medications will include: Vioxx 50mg po daily x6 days and Tylenol #3 1-2po q 3-4hrs prn. It should be clearly articulated that the paravertebral block has been shown to be safe and effective. In prior studies, patients have enthusiastically reported a high degree of satisfaction with their operative, anesthetic, and recovery experience. The interval from diagnosis to surgical treatment of breast cancer is characterized by a high degree of emotional distress. Paravertebral block can reduce these stress levels by eliminating the need for general anesthesia thereby reducing postoperative pain, nausea and vomiting, and shortening length of hospital stay. Patients undergoing breast surgery can only benefit in that they must have anesthesia, and paravertebral block can reduce the side effects they may experience.

19. Will the study be monitored? yes__x___ no_____

The study will be monitored by Harold Brem, MD., Assistant Professor, Department of Surgery, Mount Sinai Medical Center.

If yes, indicate the frequency of monitoring, specify who will do the monitoring (e.g. regulatory monitors, an external data and safety monitoring board (DSMB), a DSMB composed of local individual(s) unaffiliated with the study) and indicate to whom monitors will report in addition to the investigator (e.g. NIH, FDA, industry sponsor, IRB).

NOTE:

a) Data and patient safety monitoring: if required, a Data and Safety Monitoring Board (DSMB), which must be convened by the PI, can be made up of internal and/or

external members who have the appropriate expertise and are totally independent of and unaffiliated with the study. The composition of the DSMB should be commensurate with the complexity of the proposed study and will be reviewed by the IRB. Approval of the DSMB by the IRB is required prior to initiating the clinical trial.

b) Regulatory monitoring: if required, independent regulatory monitors must be provided by the sponsor of a project. If the PI is also the sponsor, then it is the responsibility of the PI to obtain monitors. Monitors may be MSSM personnel with the requisite expertise (documented by their curriculum vitae and approved by the IRB) or external monitors (the IRB can assist in identifying external monitors), who are not directly affiliated with the proposed study.

20. Does the principal investigator or any of the co-investigators have a potential financial conflict of interest in relationship to this study? yes___ no_x__

If yes, describe the potential conflict for each investigator.

21. Will research coordinators be employed for this study? yes__x__ no_____

a) How many coordinators will be employed for this study? 1

b) Will the coordinator work full time on this one project? yes__x__ no_____

c) How many subjects will each coordinator follow in this study: 100

d) Indicate if the individual has prior experience as a research coordinator and briefly describe that experience. Include completed course work and credentials.

The Research Coordinator has a MA from Columbia University in International and Public Affairs and has previously worked in the field of health care as a research coordinator. The Research Coordinator completed Mount Sinai's certification course in Protection in Human Subjects in Research in June 2001. He received additional training and authorization to prepare patients for completing study questionnaires and for administering consent forms.

22. Will private medical/psychiatric information be requested (e.g. in questionnaires) about individuals other than those who are the subjects who are enrolled in the study (e.g. family members)? yes _____ no ___x___

GCO # 97-368

PART I: RESEARCH PARTICIPANT INFORMATION SHEET

TITLE OF PROJECT: A randomized prospective trial comparing paravertebral nerve block and general anesthesia for surgical treatment of breast cancer

A. PURPOSE OF THE STUDY:

You are being asked to participate in a research study sponsored by the US Army Medical Research and Materiel Command. The purpose of this study is to determine whether the paravertebral nerve block, a form of regional anesthesia is an effective alternative to general anesthesia during surgery for breast cancer. You qualify for participation in this study because you have been scheduled for breast surgery for the treatment of breast cancer.

B. DESCRIPTION OF THE RESEARCH:

General anesthesia (being put to sleep with a breathing tube in place) is currently the standard method of providing anesthesia during mastectomy, lumpectomy and axillary dissection, and other operation performed in the treatment of breast cancer. It is associated with the best chance that the patient feels no pain during surgery and that the patient has no memory of the operation. General anesthesia when used for breast surgery is, however, associated with a 20 to 60% incidence of nausea and vomiting following the completion of the operation. Furthermore, while general anesthesia usually results in no pain during surgery, it cannot control surgical pain following the completion of the surgery. Therefore, following surgery most patients need narcotic pain medication, usually given through an IV or as an injection.

A promising alternative to general anesthesia is the paravertebral nerve block. This is a form of regional anesthesia similar to the anesthesia injected around the spine to ease the pain or labor in childbirth. A paravertebral nerve block is performed immediately before surgery. An anesthesiologist injects a local anesthetic, or 'numbing medicine,' close to the spine and around the nerves that supply sensation to the area of the breast and axilla (underarm). Usually seven to nine nerves are injected. These blocks are always performed while the patient is sedated or "made sleepy". The surgery is done with the patient awake, but again made sleepy with sedative medicines. The experience with paravertebral block thus far is that pain relief is usually present for 24 hours following the completion of surgery; therefore, need for pain medication after surgery is decreased. Patients having

Subject/Surrogate Initials _____

paravertebral block are also less prone to having nausea and vomiting after surgery.

This research is being done here at this institution and will be done at two other medical centers in the near future. The procedures being used in this study were developed at Duke University Medical Center where the procedure has been used extensively in the treatment of patients with breast cancer. Approximately 200 patients will be recruited to join the study, approximately 100 patients from Mount Sinai.

If you volunteer to participate in this research study, all needed tests, surgery and treatments prescribed will occur in the same manner as if you were not participating in the study. The type of surgery you are scheduled to undergo will not change.

The following will occur solely because of your participation in this research project:

1. You will be assigned by chance to have either general anesthesia or paravertebral block as the type of anesthesia used during your operation. The probability of your having one or the other is 50-50 (like flipping a coin) and will be determined entirely by chance. This process is called randomization.

2. If you are assigned to undergo general anesthesia your surgery will proceed as it would if you were not participating in the study.

3. If you have a paravertebral block, the procedure will be done in the preoperative area before you go into the operating room. After the block is placed, we will check to make sure that you are numb in the areas of the breast and underarm where surgery will be performed and will not feel pain during the procedure. You will then be taken to the operating room where you will be given medication to make you sleepy throughout the operation. The sedation medicine you will be given has a memory loss effect, which means that you may be unable to remember your time in the operating room.

4. Following your surgery, you will be taken to the recovery room. If you are not experiencing significant pain, nausea or vomiting and if you can eat and urinate without difficulty, the PI will make the clinical decision that you are able go home that same day. The criteria for making this decision will be the same for patients who received general anesthesia or the paravertebral block.

5. When you are discharged you will be prescribed pain medication by your physician which you are able to take as ordered. During the week after your surgery, we will be telephoning you once a day at a time convenient to you, to ask you questions about any

pain you are experiencing after surgery, whether you have experienced nausea or vomiting and how you are feeling in general. The questions will require approximately 15-20 minutes to answer. We will also ask you to complete a diary indicating any pain or nausea medications that you are taking at home. This will occur whether your surgery was done using general anesthesia or paravertebral block. Other than the telephone interviews and the diary, your recovery will be entirely like that of someone not participating in this study.

C. COSTS/REIMBURSEMENTS:

You or your insurance company will be responsible for the costs related to the treatment of your breast cancer. You will not receive any payment for participation in this study. There will be no additional charges to you for participating in this study above and beyond those incurred for your routine clinical care.

D. POTENTIAL RISKS AND DISCOMFORTS:

Risks of undergoing a paravertebral block:

The risks of placing a paravertebral block are:

1. In less than 1% of cases (1 out of 100) placing a paravertebral block can result in a pneumothorax (a puncture of the lung resulting in partial collapse of the lung). If this occurs, it usually requires observation only, and the problem goes away spontaneously. If it does not resolve spontaneously, a plastic tube can be placed to drain the air from the chest cavity. Placing this tube can result in temporary shortness of breath or chest pain, which can be relieved with medication. If a pneumothorax occurs your breast surgery will be delayed until the pneumothorax is resolved. If a pneumothorax occurs, it may also result in prolonged hospitalization.

2. Placement of a paravertebral block can result in epidural blockade or a temporary block of the spinal-cord which causes temporary difficulty moving and lack of feeling in the legs. This was seen in a 2 of 156 cases in a study conducted at the Duke University

Medical Center. If can also lead, temporarily, to low blood pressure or difficulty breathing. Low blood-pressure is treated by giving fluids and medication. Difficult breathing may require that a breathing tube (similar to the tube used for general anesthesia) be placed to assist your breathing as well as giving you sedation. In rare situations the breathing tube may be required for up to 24 hours after surgery.

3. There is a small risk (less than 1 out of 100) of paravetebral block causing infection at the site where the needle is inserted. This would require treatment, usually antibiotics, which may or may not be given while you are in the hospital

4. In approximately 15% (15 of 100 cases), the paravertebral block may not completely numb the area where surgery is performed, in which case you may feel some pain. This will be treated by an injection of local anesthesia by your surgeon. If your surgeon feels it is necessary, or if you request it at this time, you will be put to sleep with general anesthesia and a breathing tube will be placed. An anesthesiologist will be with you during the entire time of your surgery to ensure your comfort.

5. In very rare instances intravascular injection, or injection of an anesthetic into a blood vessel, could cause confusion, tremors or seizures. This has been reported in fewer than 1 out of 500 cases and can be controlled with medications if it occurs.

6. All medications used in this trial are approved by the United States Food and Drug Administration (FDA). Risks associated with medications used in this trial include, but are not limited to, central nervous system depression and cardio-respiratory distress. The continuous monitoring of your status by appropriate medical professionals, and the immediate availability of emergency equipment will minimize these risks.

Risks of undergoing general anesthesia:

1. The risks and complications of general anesthesia may include, but are not limited to: temporary sore throat, hoarseness, injury to teeth or airway, pneumonia, lung collapse or other lung problems, injury to arteries or veins, adverse drug reactions, awareness under anesthesia and a very small risk of brain damage or loss of life. The continuous monitoring of your status by appropriate medical professionals, and the immediate availability of emergency equipment will minimize these risks.

Risks of loss of privacy and/or personal time:

Once your physician has asked you participate in the study, you must be afforded a private room in the clinic to read this consent form, or have it read to you. This space will be made available to you for as long as you require to review this consent form in its entirety.

Subject/Surrogate Initials _____

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Prior to your surgery you will be asked to complete two questionnaires. The first questionnaire will require about 15-20 minutes of your time, and the second will require about 5 minutes of your time. In the week following your surgery you will contacted once a day at a time convenient to you to answer questions about any pain you are experiencing after surgery. These questions will require about 15-20 minutes of your time to answer. You will also be asked to maintain a daily diary of any pain or nausea medications that you are taking at home. Four weeks after your surgery you will be contacted once and asked if you have returned to work/normal activities. No further demands on your time will be made.

No data identifying you or your participation in this trial will be published or disclosed to any 3rd parties without your prior consent.

Risk of stress associated with participation:

The questionnaires you will be asked to complete were designed to permit accurate data collection while minimizing patient burden. Staff members will be available to you all times to assist with the answering of the questionnaires. Contact names and phone numbers of staff members available to answer any questions you may have are included in both questionnaire packets as well as this consent form. You may withdraw from the study at any time without jeopardizing your treatment. Your doctors may also discontinue participation if they feel that a pre-existing medical condition may prevent you from meeting the requirements of the study.

E. POTENTIAL BENEFITS:

There will be no direct benefit to you from participating in this study. However, your participation may help us determine whether general anesthesia or paravertebral block is the preferred type of anesthesia for breast surgery.

F. ALTERNATIVES TO PARTICIPATION:

If you decide not to participate in this research study, you will undergo your surgery as scheduled. The type of anesthesia used for your surgery will be based on your choice and advice from your surgeon and anesthesiologist.

Subject/Surrogate Initials _____

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From: 5/28/03 To: 9/30/03

G. CONFIDENTIALITY:

Your identity as a participant in this research study will be kept confidential in any publication of the results of this study. The information obtained during this research (Research Record) will be kept confidential to the extent permitted by law. However, this Research Record and your personal Medical Record (if any and if relevant to the study) may be reviewed by government agencies (such as the Food and Drug Administration or the Department of Health and Human Services), the agency or company sponsoring this research, individuals who are involved in, or authorized to monitor or audit, the research, or the Institutional Review Board (the committee that oversees all research in humans at Mount Sinai School of Medicine) if required by applicable laws or regulations.

H. COMPENSATION/TREATMENT:

In the event of injury resulting from your participation in this research study, short-term hospitalization and professional attention, if these are required, will be provided at the Mount Sinai Hospital, at no cost to you. Financial compensation from Mount Sinai will not be provided. If you believe that you have suffered an injury related to this research as a participant in this study, you should contact Dr. Weltz at telephone number 212-241-5148.

I. VOLUNTARY PARTICIPATION:

Participation in this study is voluntary. If you decide not to participate, this will not affect your ability to receive medical care at Mount Sinai or to receive any benefits to which you are otherwise entitled.

Any new information that develops during this study, which might affect your decision to participate, will be given to you immediately.

A signed copy of this consent form will be given to you.

Subject/Surrogate Initials _____

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J. TERMINATION OF PARTICIPATION :

You may discontinue participation in the study at any time without penalty or loss of benefits to which you are otherwise entitled. Your doctors may also discontinue participation if they feel that a pre-existing medical condition may prevent you from meeting the requirements of the study.

K. CONTACT PERSON(S):

If you have any questions, at any time, about this research, please contact either Dr. Weltz, at telephone number 212-241-5148 or John Arbo at 917-205-0071. If you still have questions you may discuss them with a member of the Institutional Review Board (the committee which oversees research at Mount Sinai School of Medicine) at telephone number 212-659-8980.

L. DISCLOSURE OF FINANCIAL INTERESTS:

NONE

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AUTHORIZATION TO PARTICIPATE IN RESEARCH

The participant/surrogate and the investigator/delegate must each **SIGN, DATE** and **TIME** this two page authorization form.

Research Subject's Name (printed):_____

1. I hereby volunteer to participate in a research program under the supervision of Dr. Weltz and her associates at Mount Sinai School of Medicine.

2. I acknowledge that I have read, or had explained to me in a language I understand, the attached consent document and that Dr. Weltz has explained to me the nature and purpose of these studies. This explanation included a description of the parts of the study that are experimental, the possible discomforts, symptoms, side effects and risks that I might reasonably expect, and the possible complications, if any, that I might reasonably experience from both known and unknown causes as a result of my participation in these studies. I have had the opportunity to ask questions I had about the study and all of the questions I asked were answered to my satisfaction.

3. I understand that I am free to withdraw this authorization and to discontinue my participation in these studies any time. The consequences and risks, if any, of withdrawing from the study while it is ongoing have been explained to me. I understand that such withdrawal will not affect my ability to receive medical care to which I might otherwise be entitled.

4. I confirm that I have read, or had read to me, this entire authorization and that all blanks or statements that require completion were in fact, properly completed before I signed this authorization.

Research Subject/Surrogate: _____
Signature

Name: _____
Print Name

Relationship: _____
If signed by surrogate

Date: _____ Time: _____

Subject/Surrogate Initials _____

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AUTHORIZATION TO PARTICIPATE IN RESEARCH (continued)

For subjects who are not able to read this consent document themselves, the following must be completed:

I confirm that I have accurately translated and/or read the information to the subject:

Name: _____
Signature

Name: _____
Print Name

Address: _____
Number and Street City State Zip Code

Date: _____ Time: _____

I confirm that the consent document was translated and/or read to the subject:

Name of Witness: _____
Signature

Name of Witness: _____
Print Name

Date: _____ Time: _____

I have fully explained to the above volunteer/patient/relative/guardian the nature and purpose of the foregoing drugs, devices or procedures, possible alternative methods of treatment which might be advantageous, the benefits reasonably to be expected, the attendant discomforts and risks involved, the possibility that complications may arise as a result thereof and the consequences and risks, if any, which might be involved in the event the volunteer/patient/relative/guardian hereafter decides to discontinue such treatment. I believe that the above volunteer/patient/relative/guardian understands the nature, purposes, benefits, and risks of participation in this research. I have also offered to answer any questions the above volunteer/patient/relative/guardian might have with respect to such drugs, devices or procedures and have fully and completely answered all such questions.

_____
Signature of Principal Investigator/Delegate (person who obtained consent)

_____
Print Name of person who obtained consent Title

Date: _____ Time: _____

Subject/Surrogate Initials _____

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